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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,059	10/17/2003	Henry R. Costantino	1733.2025-004	8156

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EXAMINER	
CORDERO GARCIA, MARCELA M	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/688,059	COSTANTINO ET AL.	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/9/07 has been entered.

Election/Restrictions

Applicant's election of Group I, drawn to claims 1-17, in the reply filed on 7/10/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election with traverse of the election of species requirement is acknowledged. The traversal is on the ground(s) that the prosecution record prior to this Office Action did indeed examine all the claims. This is found persuasive and therefore the election of species requirement is withdrawn.

Claims 1-17 are presented for examination on the merits. Claims 18-19 are withdrawn as not drawn to the elected group.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drucker (US 5,834,428) in view of Yim (US 5,385,887) and Cardinaux et al. (US 5,578,567).

Drucker (US 5,834,428) teaches a composition for sustained release which comprises, e.g., poly (lactic-co-glycolic-acid)[PLGA] which are of particular interest when it is desirable to provide a high local concentration of a GLP-2 near the pancreas to promote pancreatic growth, in diabetes, etc (e.g., column 9, lines 40-67).

Drucker does not teach the use of glycine and sucrose to the composition.

Yim discloses a composition comprising a protein (polypeptide), which is stabilized by addition of glycine and about 0.5% sucrose (which reads upon the amount and type of sugar recited in claims 7-13) [e.g., claim 4 of Yim]. The composition is incorporated into porous polymer microspheres, such as those made from PLGA (pol lactide co glycolide), a known controlled-release polymer (column 5, lines 20-21) in order to form the composition into an implant (examples, column 5-column 6). Yim also teaches using the polypeptide in an amount of 3.12-24.38% by weight (claim 4), which reads on the amount recited in instant claims 3-4. Yim teaches that the sucrose/glycine ratio can be varied to provide moisture content and bulk characteristics to the composition (e.g., column 4, lines 5-9).

Cardinaux et al. teach sustained release compositions of a peptide (column 3, lines 40-60) including PLGA (column 3, lines, 15 and 49-50), sucrose (column 3, line 33) and glycine (column 3, line 34).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of Yim by adding glycine and sucrose as taught by Yim and Cardinaux et al. The skilled artisan would have been motivated to do so because Yim (column 1 lines 5-10), Drucker (column 9, lines 40-67) and Cardinaux et al. teach sustained released compositions. There would have been a reasonable expectation of success, given that Drucker, Yim and Cardinaux et al. teach making such compositions with poly (lactic-co-glycolic-acid). The adjustment of particular conventional working conditions (e.g., determining appropriate amounts of peptide, glycine and sucrose within such method) is deemed merely a matter of judicious

selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g., optimizing the ratios of sucrose/glycine/peptide), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions in order to achieve the highest yield of the highest purity and most effective product in the most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drucker (US 5,834,428) in view of Yim (US 5,385,887), Cardinaux et al. (US 5,578,567) and Edwards et al. (Am J Physiol Endocrinol Metab).

Drucker, Yim, Cardinaux et al. are relied upon as above.

Edwards et al. teach exendin-4 is a long-acting potent agonist of the glucagon-like peptide 1 (GLP-1) receptor and may be useful in the treatment of type 2 diabetes and obesity (e.g., abstract) and treating diabetes in obese patients (page E160). Edwards et al. teach that exendin-4 is a 39 amino acid long peptide (page E155, column 2, line 9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of Drucker and Yim for the treatment of diabetes (e.g., column 9, lines 40-67) by using the peptide exendin-4 as taught by Edwards et al. (e.g., abstract) to make sustained release compositions. The skilled artisan would have been motivated to do so because exendin-4 was known as a potent agonist with potential in the treatment of diabetes, especially in obese patients (e.g., page E160) since an increase of bioavailability of is desirable to minimize dosages and optimize the treatment. There would have been a reasonable expectation of success, given that Edwards teaches that exendin-4 is a peptide and Drucker, Yim and Cardinaux et al. all teach sustained release *peptide* compositions with poly (lactic-co-glycolic-acid). The adjustment of particular conventional working conditions (e.g., determining appropriate amounts of peptide, glycine and sucrose within such method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g., optimizing the ratios of sucrose/glycine/peptide), because such

conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions in order to achieve the highest yield of the highest purity and most effective product in the most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments

As recognized by the Examiner, the Yim patent provides no teaching whatsoever regarding the use of exendin-4, or other glucoregulatory polypeptides. The Examiner attempts to cure this deficiency in the Yim patent by citing to the Hiles patent, which discloses the use of exendins for the treatment of diabetes. The sole motivation noted by the Examiner for combining the documents is the treatment of diabetes. There is no disclosure in the Yim patent that would motivate one skilled in the art to replace an

osteogenic protein with a glucoregulatory polypeptide such as exendin-4 in the compositions disclosed in the Yim patent. Similarly, there is no disclosure in Hiles et al. that would motivate one skilled in the art to incorporate exendin-4 as the biocompatible polymer with sugar and glycine.

Even if the Yim and Hiles patents could be properly combined, which Applicants do not concede, the invention as claimed does not result. As discussed above, the composition disclosed in the Yim patent includes a solubilizing agent, such as glutamic acid hydrocholoride, that ensures that a pharmaceutically effective amount of the protein can be delivered. Such a solubilizing agent is excluded from the invention as claimed by the "consisting essentially of" transitional language. Therefore, even if the composition disclosed in the Yim patent could be modified to replace the osteogenic protein with exendin-4, the claimed invention does not result because the composition would include a solubilizing agent, and therefore, would not consist essentially of exendin-4, a sugar and glycine as claimed. It would be impermissible to modify the compositions disclosed in the Yim patent to remove the solubilizing agent because that would change the principle of operation of the compositions disclosed in the Yim patent. In particular, in the compositions of the Yim patent, the solubilizing agent ensures that a pharmaceutically effective amount of the protein can be delivered. As such, modifying the compositions of the Yim patent to remove the solubilizing agent would alter the mechanism of delivery of the protein from the compositions. If a proposed modification would change the principle of operation of the prior art invention being modified, then the teachings of the reference are not sufficient to render the claims prima facie obvious

MPEP 2143.01 VI. For this reason as well, Applicants respectfully submit that this rejection cannot properly be maintained.

Response to Arguments

The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In re Herz, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original) (Prior art hydraulic fluid required a dispersant which appellants argued was excluded from claims limited to a functional fluid "consisting essentially of" certain components. In finding the claims did not exclude the prior art dispersant, the court noted that appellants' specification indicated the claimed composition can contain any well-known additive such as a dispersant, and there was no evidence that the presence of a dispersant would materially affect the basic and novel characteristic of the claimed invention. The prior art composition had the same basic and novel characteristic (increased oxidation resistance) as well as additional enhanced detergent and dispersant characteristics.). "A consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco,

Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also AK Steel Corp. v. Sollac, 344 F.3d 1234, 1240-41, 68 USPQ2d 1280, 1283-84 (Fed. Cir. 2003) (Applicant's statement in the specification that "silicon contents in the coating metal should not exceed about 0.5% by weight" along with a discussion of the deleterious effects of silicon provided basis to conclude that silicon in excess of 0.5% by weight would materially alter the basic and novel properties of the invention. Thus, "consisting essentially of" as recited in the preamble was interpreted to permit no more than 0.5% by weight of silicon in the aluminum coating.); In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) ("Although consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with

the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of' language.") [MPEP 2111.02]. In the instant case, both the instant and the Yim composition are drawn to sustained release compositions, therefore, the presence of a solubilizer does not alter the instantly claimed basic and novel characteristics of the composition (i.e., sustained release). Additionally, the Cardinaux et al. patent teaches that inclusion of glycine and sucrose within such PLGA sustained release peptide compositions is well within the skill of one of ordinary skill in the art as mentioned above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 7,164,005 in view of Yim (US 5,385,887) and Cardinaux et al. (US 5,578,567). Although the conflicting claims are not identical, they are not patentably distinct from each other because The instantly claimed invention and the invention claimed in Application '808 are both drawn to compositions for sustained release of a biologically active polypeptide consisting essentially of a biocompatible polylactide-co-glycolide polymer having dispersed therein a biologically active glucoregulatory polypeptide (e.g., exendin-4, see claim 2 of US '005. US '005 does not teach further adding glycine. Yim and Cardinaux et al. are relied upon as above.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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